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Technology for the industrial production of K3 series vitamins based on menadione

An improved technology for the industrial production of K3 series vitamins based on menadione is reported. The procedure involves the Cr(VI) — promoted oxidation of the corresponding methyl-naphthalenes with the following purification by precipitation/recrystallization. The best results were obtained under the process temperature between 20–40 °C, solution pH after dilution of MNB in a range of 5.5–5.7, and MNB content in initial solution of 25–30%.

Keywords: Vitamin K3; methyl-naphthalenes; Cr(VI) — compounds; menadione; industrial scale

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Introduction

For the industrial production of vitamins of the K family, the most accessible and important precursor is 2-methylnaphthalene-1,4-dione, (menadione) [1]. In some sources, menadione is called vitamin K3 [2], although derivatives 1,4-naphthoquinone are not natural chemicals and therefore cannot be qualified as vitamins. Menadione can be considered as provitamin due to the possibility of its metabolism in the human body into vitamins K2, menaquinones, [3] containing various alkyl fragments at the position of C3 of the naphthalene-1,4-dione.

According to the literature, the simplest and most cost-effective industrial method for producing menadione in the form of sodium bisulfite (MSB) or nicotinamide bisulfite (MNB) is the Cr(VI) compound-mediated oxidation reaction of 2-meth-

ynaphthalene-containing raw materials in an acidic medium with the release of menadione as an intermediate product [4], and the subsequent crystallization of the MSB from water or the precipitation of nicotinamide MNB from the mother liquor. Since 2012, a domestic technology implemented according to this principle has been developed at the Novochrom LLC enterprise (Novotroitsk, Orenburg Region). The main problem of this technology is associated with a strict restriction on the content of impurity components in final consumer products, such as K3 series vitamins. For example, EU Regulation No. 1831/2003 limits the chromium content in sodium menadione bisulfite to 45 mg/kg, and in the menadione nicotinamide bisulfite 142 mg/kg. Even trace amounts

of 2-methylnaphthalene, 1-methylnaphthalene, indole(s) are also excluded.

In connection with the above, the initial stages of industrial production of K3 series vitamins are burdened with a significant accumulation of substandard and intermediate products, as well as high costs for their recycling. Namely, the level of such important technical and economic

indicator, as the volume of substandard MNB with a chromium content from 300 to 2500 mg/kg in an amount of more than 30 tons for 2016 makes the industrial production of K3 series vitamins to be not competitive in the global MSB market [5]. The aim of this work was to develop a methodology for the processing of menadione nicotinamide bisulfite on an industrial scale.

Experimental part

Research Methodology

Industrial grade MNB with a chromium content of 2250 mg/kg was used for research. Sulfuric acid, sodium carbonate, butanol-1 of technical grade were purchased from commercial sources. Analytical researches were carried out according to the methods certified by Novochrom Ltd.

Investigations of the method of processing MNB by carrying out the reactions of direct and reverse synthesis

50 g of MNB was re-pulped in 125 ml of water containing 12 ml of butanol-1. Sodium carbonate was slowly, in small portions, added to the resulting suspension to achieve a stable pH of 5.5–5.7. The reaction volume was maintained until the MNB was completely dissolved, followed by filtration to remove insoluble particles. After the filtration the obtained solution was acidified with 65% sulfuric till the pH of 2.0–2.2. The precipitated MNB was filtered, washed and air-dried.

Investigation of the influence of the pH on the fractionation size of the impurities

The influence of the pH of the medium on the fractionation size of chromium-containing impurities was checked similarly to the first method, except that before filtering the pH of the solution was reduced to 4.5 with the following addition of 5 g of diatomite to improve filtration.

Investigation of the cyclic method of MNB processing

To study the cyclic processing process, 50 g of MNB was re-pulped in 125 ml of water containing 12 ml of butanol-1. Sodium carbonate was slowly, in small portions, added to the resulting suspension to reach a stable pH value in a range of 5.5–5.7. The reaction volume was maintained until the MNB was completely dissolved. The pH of the solution was reduced to 4.4–4.6 by the addition of 65% sulfuric acid. After that the 5 g of diatomite was added, and the insoluble particles were filtered out. The filtered solution was acidified with 65% sulfuric acid till the pH of 2.0–2.2, and the resulted solution was stirred for 15 minutes. After the filtration the precipitate was washed and dried. The next cycle was carried out similarly to the first one, except using a filtrate after the separation of the MNB instead of water. At the end of the third cycle, all the washings and the filtrate were collected together and made alkaline with sodium bicarbonate to reach a pH of >10, followed by filtration and washing of the precipitated menadione.

Investigation of the influence of water amount on the chromium content in the recycled MNB

The study of the effect of the amount of water on the fractionation of chromium

was carried out according to the methodology of the first cycle of the cyclic process,

except that the amount of water was 50, 80, 100 and 130 ml.

Results and discussion

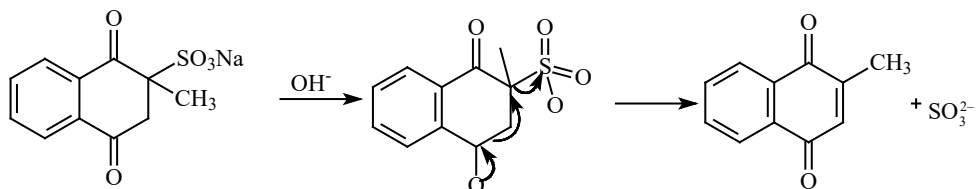
The technology for producing K3 vitamins consist of three separate stages: synthesis of menadione with Cr(VI) compounds, isohydric crystallization [6] of MSB, and the precipitation of MNB by reaction of the mother liquor with nicotinamide in an acidic media. Based on the classical positions of fractionation of impurity components in the isohydric crystallization mode [6], we refined the dependence of the solubility of MSB in water in the operating temperature range and compiled a nomogram for assessing the possible effects of purification from chromium during crystallization [7].

We have previously shown that the use of additives of water-soluble aluminum salts [8] leads to a decrease in the chromium content during the synthesis of MSB,

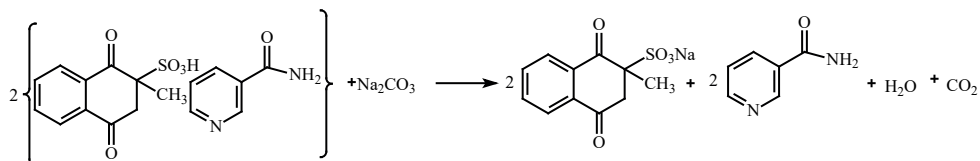
while using liquid extraction with butanol-1 leads to the production of high-quality MNB [9].

The return of substandard MNB to the scope of implementation is expected to be achieved through the sequential processes presented in schemes 1–3.

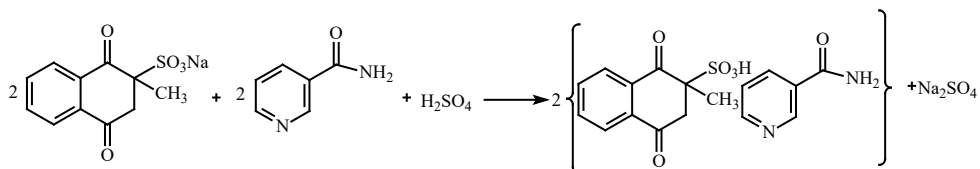
The dissociation of MNB into the starting reagents under the action of alkaline reagents, in particular sodium carbonate in the pH range of 5.5–5.7 (Scheme 1), makes it possible to efficiently obtain a solution of MSB and nicotinamide, as well as impurities, which are highly soluble in water. A further decrease of the pH of the medium to 4.4–4.6 leads to the precipitation of chromium-containing impurities, the removal of some of which from the solution was made by the filtration, and



Scheme 1. Decomposition of MNB into the starting reagents



Scheme 2. Synthesis of MNB



Scheme 3. Dissociation of MSB to menadione

this step was followed by the direct synthesis of MNB. This allows to obtain a product with a chromium content of less than 142 mg/kg. Processing the mother liquor after the separation of MNB with alkaline reagents allows additional extraction of MSB menadione and its return to the stage of the synthesis of MNB. The cleavage of MSB to menadione was carried out by the action of alkaline reagents at a pH of more than 11. It should be noted that earlier it was shown that in the pH range from 6 to 10 the equilibrium is shifted towards the formation of MSB [10].

From the data collected it follows that the sequential reverse reaction of the cleavage of MNB into initial products at a pH of 5.5–5.7 with filtration of undissolved particles, followed by a direct synthesis reaction, leads only to a slight decrease in the chromium content in the final product.

In the course of studies, it was found that when alkaline reagents, in particular sodium carbonate and sodium bicarbonate, are added to the suspension of the initial MNB to adjust a pH to 5.5–5.7 all MNB decomposes into the starting products. When the solution is acidified with sulfuric acid to adjust a pH of less than 5.0 a fine precipitate is formed. The precipitation of MNB usually begins at the pH

of the solution of less than 4.2. Studies, carried out with a high dilution of the solution to prevent the deposition of MNB, showed that the precipitation of the impurities continues until the pH of the solution is reduced till 2.9–3.0, and with further acidification no precipitation is observed. Also, the color of the solution changes from dark brown at pH 5.6 to light yellow at pH 2.5, after filtering the precipitate of impurities. To avoid precipitation of MNB at pH less than 4.2, the precipitation of impurities was carried out in a range of pH range of 4.4–4.6.

From the results of cyclic processing it follows that it is not possible to obtain MNB using the filtrate from the previous stage with a low chromium content while maintaining the regime of the first cycle. Apparently, an increase in the salt content of the solution leads to a different distribution of the impurity between the aqueous and organic phases. This is confirmed by the fact that dilution of the solution of the second cycle after the filtration of the insoluble residue leads to cloudiness of the solution and precipitation of the impurities. From the results of a study of the effect of the amount of water on the chromium content in the final MNB it follows that an increase in the amount of water leads to a decrease in the chro-

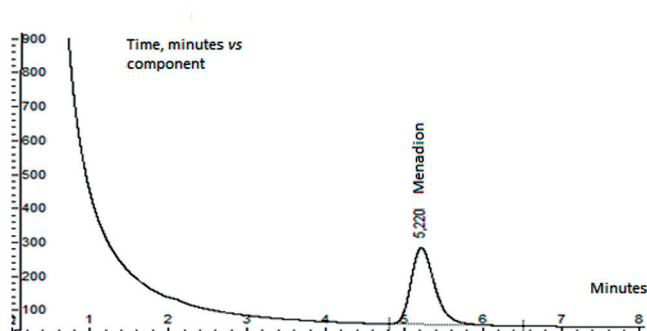


Fig. 1. Chromatogram of the processed MNB

mium content in the final product due to a more complete deposition of chromium-containing impurities from the solution upon decreasing pH. Additional extraction of menadione from the mother liquor is achieved by changing the pH of the medium above 10.0 by adding sodium carbonate.

Conclusions

In conclusion, a technical solution is developed for the processing of menadione nicotinamide bisulfite with a high content of chromium and organic impurities, as well as for one with an expired shelf life to produce a high quality menadione with low chromium content. The best results were obtained at the temperature of the reaction mixture of 20–40 °C, the pH

Chromatographic studies of the resulting MNB (Fig. 1) to demonstrate the absence of 2-methylnaphthalene and other organic impurities in it, which confirms the effectiveness of the described purification method.

after dilution in a range of 5.5–5.7, and the initial MNB content of 25–30%. This technical solution is also applicable well for the accumulated previously substandard commercial products, and it finalizes the cycle of the improvement of the existing industrial production of K3 series vitamins based on menadione.

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